Decoding Genetic Insights:
Navigating Possible Test Results

Understanding your genetic test results for conditions like Marfan, Loeys-Dietz, or VEDS can be challenging. Here's a simple Q&A to help make sense of what your results may mean and what you might consider doing next.

Q: What does a positive genetic test result mean?

A: A positive result means a genetic variation that can cause a genetic condition has been found. Think of genetic variation as a change in the spelling of a gene. You may see this called a pathogenic or likely pathogenic variant. You may also see this called a mutation. A positive result typically confirms the diagnosis if the variation matches your clinical diagnosis. Sometimes, it may indicate a different condition than was initially thought (although usually, this would be a similar or related condition), potentially affecting your risks and medical care.

A positive result allows family members to have cascade testing. Cascade testing is a process where family members are tested for the same genetic variation, helping to determine their risk of having the condition or passing it on to their children.

Q: What if the test result is negative or uninformative?

A: A negative result means no known variations were found in the genes tested - but it doesn't always mean there is no genetic condition, as there could be variations in other genes not tested for or limitations in the test's ability to find your family's specific genetic variation. This is why calling this an "uninformative" test may be more accurate.

This can be a frustrating or confusing result for those seeking answers. In the context of aortic disease, it's important to understand that a negative or uninformative result is quite common. In fact, overall, the specific genetic variation responsible for a personal history of thoracic aortic aneurysm is only identified about 20% of the time. So, if your test results don't provide clear answers, you're not alone in this experience.

In such cases, you might think about more tests for different gene changes, especially if your signs point to a genetic condition that wasn't initially tested for. Alternatively, you may have had uninformative testing years ago – new gene discoveries and improved technology may have increased the likelihood of finding your family's specific mutation now. Talking with a doctor or genetic counselor can help you decide if more tests are a good idea for you.

If a family member who is thought to have the condition tests negative, it's usually not recommended for other family members to undergo genetic testing (although echocardiograms or other imaging for potentially at-risk family members may be recommended). However, a negative result in cascade testing (when the family's mutation has already been identified) typically means the person's risk is similar to the general population for that condition (in other words, they haven't inherited the condition that runs in the family).

"Genetic testing can not only help us find a gene variant to use for testing family members and figuring out who is at risk, but results can also help us to "tweak" your healthcare, providing specialized medical management based on the specific gene, and possibly the variant, detected."

~Gretchen MacCarrick, MS, CGC, a genetic counselor at Johns Hopkins and professional advisory board member for the Foundation.

Q: How should I interpret a Variant of Uncertain Significance (VUS)?

A: A VUS is a genetic change that's effect on condition risk is not clear. It doesn't confirm or rule out a genetic condition. Over time, as more research is done, the classification of a VUS might change. It's important not to use a VUS for making medical decisions, as its significance is not clear.

Testing of family members for a VUS is generally not recommended and wouldn't be helpful outside of specific situations where your family could help scientists learn more about the VUS. The lab or genetics professional involved would help to coordinate this, if applicable.

Q: Can the interpretation of genetic test results change over time?

A: Yes, as genetic research advances, interpretations of test results may evolve. This is especially true for VUS, where new information can change how these variants are viewed. It's essential to keep up-to-date and talk with your healthcare provider about any new information.

Q: What are the next steps after receiving genetic test results?

A: Discuss your results with your doctor or genetic counselor. They can help you understand what the results mean in relation to your health and family history, and suggest the next steps. This might include specific medical care, lifestyle changes, or more genetic testing for you or your family. Genetic testing is just one part of managing and understanding your health.

**Information in this article is provided by The Marfan Foundation. Quote provided by Gretchen MacCarrick, MS, CGC.*